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Epidemiology, Treatment, Survival and Prognostic Factors of Cutaneous Mucoepidermoid Carcinoma: A Distinct Entity with Indolent Clinical Course

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Primary cutaneous mucoepidermoid carcinoma (cMEC) is a rare neoplasm with mucus-secreting and epidermoid cells on histology¹. Its etiopathology remains unclear and it is postulated to arise de novo or from pre-existing nevus sebaceous, sweat glands, or ectopic salivary glands². Clinically, cMEC may mimic a basal cell carcinoma, particularly if ulcerated, and dermatologists must first rule-out metastatic disease, salivary origin, and distinguish cMEC from more aggressive adenosquamous carcinoma (cASC). Current literature on cMEC is limited to case reports and single-institution studies. Given the rarity of this tumor, lack of established treatment guidelines, and uncertain aggressiveness which may be in part due to misdiagnosis as cASC, an in-depth national study can better characterize pertinent epidemiologic and prognostic factors associated with cMEC.

After approval by the Yale Human Investigation Committee, and with adherence to STROBE guidelines¹, data on patients with a diagnosis of primary cMEC (histology code

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ⁱⁱAs age is defined as a continuous variable in this dataset, the hazard ratio reflects the increased risk of death for each additional year of life.

8430/3) were obtained from the SEER database for the years 1973 to 2016. Data was collated and analyzed as reported previously³.

A total of 89 patients with cMEC were identified. The majority occurred in individuals of white race (80.0%), with slight preponderance for male sex (55.1%) and mean age of diagnosis of 63.4 years (range 23–94). Most (68.6%) cases presented with local (stage I) disease and were low grade (75.5%). The most frequent site of presentation was the face (84.3%). Treatment modalities included surgery in 81.8% of cases, radiation (15.7%), and chemotherapy (6.8%). Detailed descriptive statistics are provided in supplementary material (Mendeley doi:10.17632/3g58dntvd.1).

Five-year OS and DSS for patients with cMEC were 68.2% and 76.0%, respectively (Figure 1). Predictors of survival on univariate analysis included older age (shorter OS and DSS), high lesion grade (shorter OS), face as lesion site (longer OS and DSS) and surgical resection (longer OS and DSS). In risk-adjusted models, independent predictors of survival were older age and high grade (shorter OS and DSS), lesion location on the face (longer OS and DSS) and receipt of surgery (longer DSS)(Table 1).

Our study provides insight into nation-wide epidemiology, prognosis, and treatment for cMEC. On risk-adjusted model surgical resection was a predictor of DSS, supporting its use in management, whereas the understanding of the utility of chemotherapy and/or radiation therapy is limited based on unmeasured biases in coding this specific data. Our data also support literature demonstrating that cMEC is an overall low-grade neoplasm distinguishable from more aggressive cASC, and that it may benefit from surgical resection^{4,5}. In particular, Nouri et al. have reported success with the use of Moh's micrographic surgery for treatment of cMEC on the face⁴.

Limitations in this study design include a potential for absent or incorrect reporting of retrospective data, including misclassification bias from potentially overlapping cancer terms, migration of patients in and out of SEER registry areas, potential over-representation of data from academic centers and changes in coding practices over time. Despite such limitations, our study presents the first available population-level data on cMEC. Determinants of survival include: age, cancer grade, lesion location, and receipt of surgical intervention. Although a rare tumor, physicians should be cognizant of the pertinent epidemiologic, therapeutic, and prognostic factors which may guide management.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Abbreviations

cMEC Cutaneous mucoepidermoid carcinoma

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DSS	Disease-specific survival
HR	Hazard ratio
OS	Overall survival
PY	Person-years
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
SEER	Surveillance, Epidemiology and End Results
US	United States

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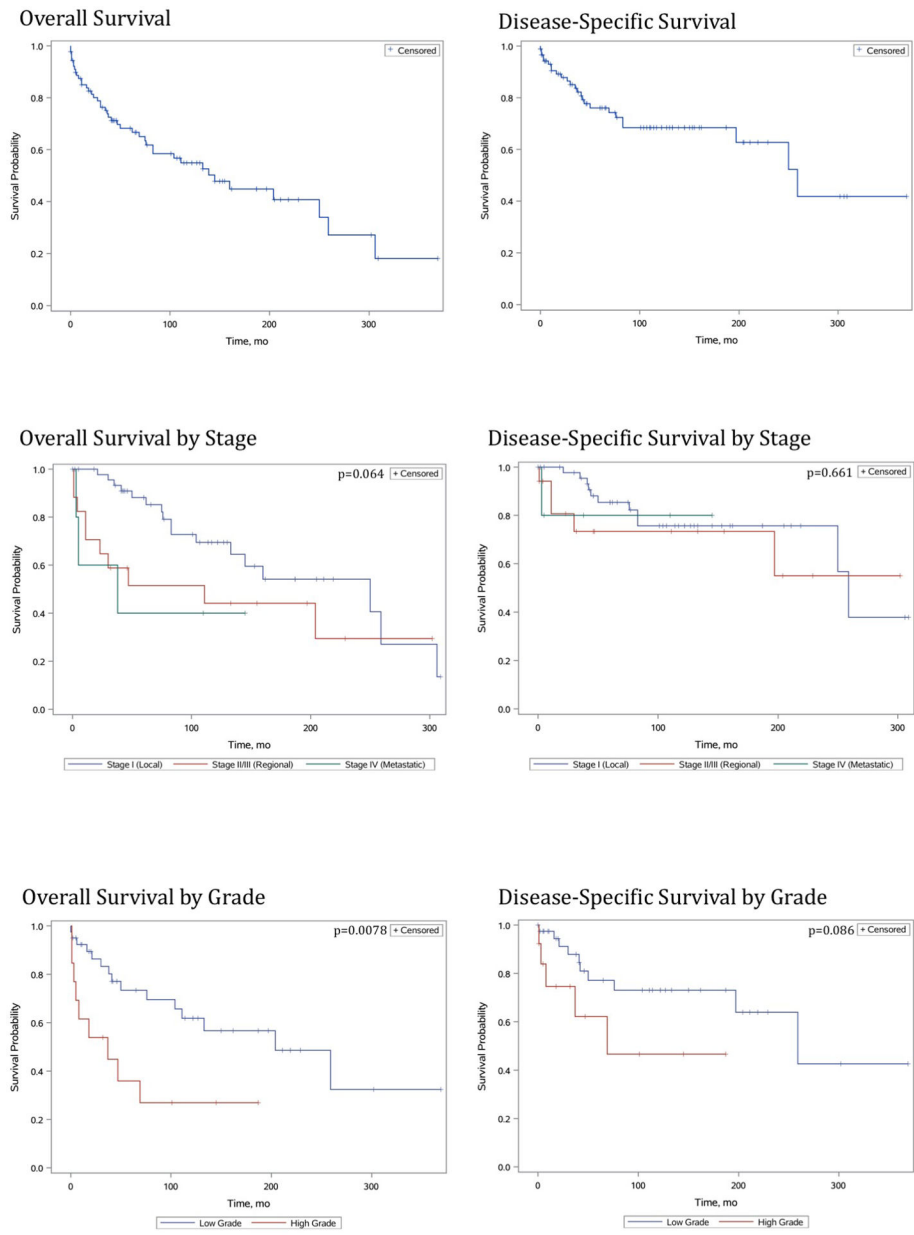


Figure 1. Malignant cutaneous mucoepidermoid carcinoma. Survival analysis using Kaplan-Meier analysis.

Table 1.

Univariate and multivariate analysis of overall and disease-specific survival.

Characteristic	Overall		Disease-Specific	
	HR (95% CI)	P Value	HR (95% CI)	P Value
Univariate ^a				
Year of diagnosis (Advanced)	1.01 (0.98–1.05)	0.60	1.03 (0.98–1.08)	0.27
Age (Older)	1.07 (1.04–1.10)	<0.0001	1.07 (1.03–1.10)	<0.0001
Sex (Male)	1.35 (0.73–2.51)	0.34	1.20 (0.54–2.65)	0.65
Race (White)	1.03 (0.43–2.50)	0.94	0.98 (0.33–2.88)	0.96
Residency demographic (Rural)	1.00 (Reference)		1.00 (Reference)	
Urban	0.47 (0.21–1.06)	0.06	0.60 (0.24–1.51)	0.27
Metro	0.66 (0.32–1.37)	0.27	0.31 (0.11–0.89)	0.03
Stage (Higher)	1.50 (1.04–2.17)	0.03	1.24 (0.70–2.19)	0.46
Grade (High)	3.02 (1.28–7.14)	0.01	2.62 (0.85–8.07)	0.09
Body site (Trunk or Extremities)	1.00 (Reference)		1.00 (Reference)	
Face	0.33 (0.14–0.76)	0.009	0.27 (0.10–0.72)	0.009
Surgery (Performed)	0.38 (0.19–0.77)	0.007	0.22 (0.10–0.53)	0.0006
Radiation therapy (Received)	1.61 (0.77–3.40)	0.21	1.12 (0.38–3.30)	0.83
Chemotherapy (None)	0.21 (0.08–0.56)	0.002	0.15 (0.05–0.47)	0.001
Multivariate ^{a*}				
Year of diagnosis (Advanced)	1.01 (0.95–1.07)	0.76	1.05 (0.96–1.14)	0.28
Age (Older)	1.09 (1.05–1.14)	<0.01	1.08 (1.03–1.14)	<0.01
Sex (Male)	0.48 (0.17–1.35)	0.17	0.40 (0.11–1.54)	0.18
Grade (High)	8.49 (2.46–29.3)	<0.01	6.86 (1.40–33.63)	0.02
Body site (Face)	0.11 (0.03–0.45)	<0.01	0.08 (0.01–0.45)	<0.01
Surgery (Performed)	0.56 (0.19–1.64)	0.29	0.23 (0.06–0.86)	0.03

^aCategory in parentheses defines the strata the hazard ratio represents.

* Variables were chosen for the multivariate model using forward and backwards stepwise selection using an entry of 0.3 and stay of 0.15.